Apr 24th, 1:30 PM - 2:30 PM

Nurse's Perceptions of Best Practices to Assess Pediatric Patients and Educate Their Families Experiencing Delayed Effects of Cancer Therapy: "Chemo Brain:" A Pilot Study

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December 10, 2014

Abstract

With more advanced and more aggressive chemotherapy cancer treatment leading to higher survival rates, complications with quality of life are becoming more prominent. Of these complications, delayed cognitive processing, commonly known as "chemo brain," is becoming a topic of interest. Cognitive changes are some of the most common as well as most challenging complications associated with central nervous system (CNS) directed treatment, such as intrathecal chemotherapy, for acute lymphoblastic leukemia (ALL) and brain tumors. The term "chemo brain" is often used to describe self-reported or observed cognitive processing delays in patients who receive chemotherapy as a form of cancer treatment (Raffa, 2009). Although these cognitive delays have the potential to be serious side effects, little education is given to the patients and families regarding these possibilities prior to the initiation of cancer treatment. The purpose of this paper is three fold: 1) to define and discuss the etiology of "chemo brain," 2) discuss the best assessment and evaluation of severity of "chemo brain," and 3) to explore pediatric oncology nurses reports of practice implications for teaching and supporting pediatric patients and their families experiencing "chemo brain." A theoretical framework that will guide the research is Erikson's Theory of Psychosocial Development with a focus on the school age stage of industry versus inferiority. With the possible gap in knowledge and skill that may be present in these children who have undergone chemotherapy, there is a significantly higher chance of them developing a sense of inferiority rather than the preferred sense of industry. Convenience and snowball sampling will be used to locate pediatric oncology registered nurses to complete the research instrument. This pilot study has a qualitative/descriptive design with a goal of 30 subjects. Research data will be

collected through a short survey created by the primary investigator that has construct and content validity from two advanced practice pediatric oncology nurses.

Acknowledgements

I would like to acknowledge and thanks my parents, Jon and Janis Tapping, for supporting me in every way possible throughout my education. I would also like to acknowledge my late Nana who instilled in me the caring personality that comes with being a nurse. Her picture above my desk gives me motivation everyday to become as good and as caring of a nurse as she was. Lastly, I would like to thanks Dr. Luanne Linnard-Palmer for supporting me throughout the research process.

Introduction

With more advanced and more aggressive chemotherapy cancer treatment leading to higher survival rates, complications with quality of life are becoming more prominent, especially delayed cognitive processing, commonly known as "chemo brain." At diagnosis and throughout treatment, patients and families are routinely educated about the plan of care, but according to oncology nurses' reports, too often details regarding the possibility of cognitive declines or deficits are left out.

Background

Cognitive changes are some of the most common as well as challenging complications associated with central nervous system (CNS) directed treatment, such as intrathecal chemotherapy, for acute lymphoblastic leukemia (ALL) and brain tumors. The estimated incidence of patients who experience deficits in cognitive processing related to their CNS directed treatment is approximately 20% to 40% for children with ALL and

40% to 100% for children with brain tumors (Moore et al., 2013). The term "chemo brain" is often used to describe self-reported or observed cognitive processing delays in patients who receive chemotherapy as a form of cancer treatment (Raffa, 2009). The clinical manifestations of "chemo brain" can "affect multitasking, create stress, and weaken performance when patients are challenged by high-level cognitive demands" (Staat & Segatore, 2005).

Purpose

The purpose of this paper is three fold: 1) to define and discuss the etiology of "chemo brain," 2) discuss the best assessment and evaluation of severity of "chemo brain," and 3) to explore pediatric oncology nurses reports of practice implications for teaching and supporting pediatric patients and their families experiencing "chemo brain" (CB).

Literature Review

Introduction

"Chemo Brain" (CB) is a term used to describe the general cognitive deficit that results from cancer chemotherapy treatment. According the Evens & Eschiti (2009), CB can be simply described as "dysfunction, weakening, or impairment" of the memory in patients who have undergone chemotherapy treatment for cancer. Raffa et al. (2006) suggested that these impairments can be self-reported or observed. A more specific definition of CB stated that it presents as "weakened cognitive abilities, speed of information processing or reaction time, and organizational skills" along with the negative impact on "language ability, memory, concentration, and attention" (Staat & Segatore, 2005). Many of these core symptoms have been termed "executive functions,"

mainly including the "ability to allocate attentional resources and to plan and organize behavior" (Mulhern & Palmer, 2003). Although theses deficits may seem to cause deteriorating effects, it is suggested that "young children aren't actually dementing, but rather are not acquiring new information and skills at an appropriate age" (Duffner, 2009)

According to Staat & Segatore (2005), the patient's quality of life may be significantly affected because of the severity of the CB symptoms. Cognitive deficits may be subtle enough so only the patient and close relatives notice, but they also may be severe enough to cause others to notice – which is noted to be most difficult for the patient as well as their family and close friends.

Moore et al. (2013) and Evens & Eschiti (2009) both presented the statistic that as many as 40% of pediatric acute lymphoblastic leukemia (ALL) patients who are treated with chemotherapy alone will report CB. Overall, studies have shown that cognitive difficulties affect 25%-35% of all patients that undergo systemic chemotherapy (Evens & Eschiti, 2009).

Deficits of CB often appear over time rather than right away. In fact, myelination changes in the central nervous system (CNS) from a chemotherapy drug, 5-fluorouracil can be delayed for several months and may become progressive (Evens & Eschiti, 2009). By the late 1990's, reports began to suggest that children who were treated for ALL without cranial radiation therapy but with chemotherapy developed progressive cognitive declines 3-4 years following the completion of their chemotherapy (Duffner, 2009). More detrimental, it has been suggested that in a small minority of patients, CB is still perceptible 10 years after the completion of treatment (Staat & Segatore, 2005).

Etiology of "Chemo Brain"

The deficits of CB are believed to occur because of alterations in the blood-brain barrier (BBB), vascular injury, and myelination changes. With this BBB impairment, toxic agents are allowed access to the brain more readily and in normal circumstances where entry would not usually happen (Evens & Eschiti, 2009). In addition to these abnormalities, Mulhern & Palmer (2003) suggested that the late effects might also include diffuse and multifocal white matter abnormalities, microvascular occlusion, and calcifications. While Raffa (2009) stated that mainly white matter abnormalities were related to chemotherapy treatment, Evens & Eschiti (2009) discussed how researchers have also shown a decrease in the brain's grey matter along with the demyelination of white matter fibers following chemotherapy treatment. In neuroimaging studies discussed by Raffa (2009), changes were evident at about two months then appeared to plateau at about six months and persisted for the duration of the study (which was about one year).

Staat and Segatore (2005) discussed three possible mechanisms that cause CB: direct neurotoxicity, inflammatory mechanisms, or a vascular mechanism. The theory of direct neurotoxicity implies that chemo agents cause direct toxicity to the brain, producing demyelination. The theory of an inflammatory response has to do with chemo agents destroying healthy cells in addition to cancer cells. This destruction of healthy cells produces a physiologic stress and the brain interprets the inflammatory response and the increase release of cytokines as stress, which may result in a decreased ability to learn, memory difficulties, and poor concentration (Evens & Eschiti, 2009). The last theory involves a vascular mechanism where injury obstructs the microvasculature of the brain, causing ischemia or infarction of dependent brain tissue leading to the deficits of CB (Staat & Segatore, 2005).

Because cancer treatment is often multimodal, it is important to understand that both chemotherapy and radiation may be used. If this is the case, it makes it very difficult to separate the adverse effects (Raffa et al., 2006). According to Evens & Eschiti (2009), Cyclophosphamide and 5-fluorouracil are two of the most commonly used chemo drugs that can readily cross the BBB. Because of this, they are thought to significantly contribute to CB. Although chemo drugs such as methotrexate (MTX) and vincristine are not believed to penetrate the BBB, they are believed to play a role in altering its permeability, which allows the drugs to gain entry to the brain, also contributing to CB. According to Staat & Segatore (2005), cyclophosphamide, MTX, and fluorouracil in high doses are known to have the strongest association with the development of CB. As expected, more cognitive impairments were noted in patients who were given high doses of chemo compared to a standard dose, and more cognitive impairment was seen in patients given a standard dose of chemo than in control groups (Raffa et al., 2006). High dose chemotherapy, especially with MTX, has been associated with the previously discussed white matter injury (Mulhern & Palmer, 2003).

There are many risk factors and contributing factors relating to CB. Both Duffner (2009) and Mulhern & Palmer (2003) discussed the finding that early age at diagnosis and chemotherapy treatment has consistently been identified as a major risk factor for developing CB. Mulhern & Palmer (2003) also discussed how being of female gender confers a greater risk for developing CB. They also stated that the factors of early age at diagnosis and start of chemo treatment along with low socioeconomic status were associated with more severe CB in females, but did not reliably correlate in males. It has

also been suggested that people who carry the APOE e4 gene (a gene associated with Alzheimer's) may be more susceptible to CB (Evens & Eschiti, 2009).

Assessment of Severity

Deficits of CB may me subtle, so they may only be noticeable to the patient and family and not to the health care team. Evens & Eschiti (2009) provided the statistic that only 38% of nurses assessed patients for CB. While longitudinal evaluation of cognitive functioning for childhood cancer survivors is not yet considered standard of care, many pediatric oncology programs emphasize cognitive assessment for high-risk patients (Ullrich & Embry, 2012).

Because there may be different contributing factors to the cognitive decline, there are differential diagnoses that must be ruled out in order to conclude that the deficits are caused by the chemotherapy (Evens & Eschiti, 2009). According to Staat & Segatore (2005), observational assessment is the most appropriate method to screen for CB.

The neurocognitive assessments are essential in facilitating access to the necessary special education services and in tracking the child's development over time. Ullrich & Embry (2012) suggested that a comprehensive neurocognitive assessment should focus on global intellectual functioning and academic achievement along with other specific high-risk areas of deficit. They also discussed the recommendation that high-risk survivors should be evaluated when they transition into a long-term follow-up program. This should be done both to detect subtle impacts on overall functioning and to serve as a baseline for future assessments since it is known that CB late effects can progress over time. This reevaluation should look at factors such as academic

performance, any acute changes or new difficulties, and the individual child's specific risk factors.

Ullrich & Embry (2012) also provided a table providing commonly used assessment tools for assessing specific neurocognitive domains in children. To assess global cognitive functioning (IQ), the WISC-IV is often used. The CPT-II or Trail Making Test Part A are often used to assess attention. The CMS may be used to assess memory. Processing speed may be assessed by the WISC-IV Coding/Symbol Search. Executive functioning may be assessed by a few tests, including the BRIEF or the Trail Making Test Part B. Finally, academic achievement may be assessed by the WIAT-III or WJ-III assessment tools.

Practice Implications

According to Mulhern & Palmer (2003), interventions can be divided into two approaches: those that aim to avoid or reduce the neurotoxicity of the CNS therapy, and those that aim to minimize or rehabilitate deficits that are not preventable. First, in order to determine potential interventions, the cognitive deficits must be distinguished from brain metastases and other medical conditions (Evens & Eschiti, 2009). The earlier the deficits are recognized and attributed to chemotherapy treatment, the earlier potential treatments can begin.

One of the first implications of practice is education. Nurses play a significant role in educating patients and families about the diagnosis, treatments, and potential side effects. According to Staat & Segatore (2005), there is a huge debate about whether or not the risk of CB should be disclosed during the consent process. On one hand, when a treatment regimen has a known central neurotoxicity, it is

required to provide informed consent. On the other hand, there is limited knowledge regarding CB, and the incidence of CB must be confirmed before including it in routine discussion and as part of the informed consent process. Patients and families who have experienced CB first hand emphasized the desire for full disclosure or risks, including the potential for CB (Staat & Segatore, 2005). Education can allow patients to cope more effectively and the resulting awareness may be able to provide some sense of control and encourage the family to connect with an appropriate resource. As of 2009, there were no nationally known support groups for CB, so the pediatric oncology nurse should strongly consider finding a way to develop local groups (Evens & Eschiti, 2009).

Another intervention that is suggested to improve cognition during CB is exercise. Evens & Eschiti (2009) stated that because exercise improves blood flow and oxygenation to the brain, it might lead to improved cognitive functioning. They also stated that acupuncture has recently been shown to dilate cerebral blood vessels, which improves circulation as well as increases oxygenation to the brain.

When the non-pharmacological interventions are not sufficient, there are some proposed pharmacological interventions to minimize the deficits of CB. Both Ullrich & Embry (2012) and Staat & Segatore (2005) mentioned the use of methylphenidate (Ritalin) as an option to help with inattention, organizational skills, as well as forgetfulness. Both Evens & Eschiti (2009) and Staat & Segatore (2005) discussed the use of erythropoietin and epoetin alfa. These drugs are used to treat chemotherapy-induced anemia – they increase the oxygen carrying capacity of blood, which in turn can lead to decreased ischemia and hypoxia in the brain,

leading to cognitive improvement. Both sources also discuss the use of Gingko Biloba. This herb is thought to have a neuroprotective, antioxidant, and membrane-stabilizing effect as well as possibly inhibiting the loss of cholinergic receptors, which are known to have an impact on memory and cognition (Staat & Segatore, 2005).

Theoretical Framework

A theoretical framework that will guide the research is Erikson's Theory of Psychosocial Development. In this theory, Erikson divides the "life cycle" into eight stages, and the focus of this project will be on the school-age stage of Industry versus Inferiority. During this stage children will either begin to develop a sense of pride in their accomplishments and abilities (industry) or will doubt their ability to be successful (inferiority). According to Erikson (1950), when a child develops a sense of industry, bringing "a productive situation to completion" is a goal that will gradually "supersede the whims and wishes of play". Simply put, the child will feel great satisfaction from completing a task. Erikson also discusses the danger of this stage, feelings of inadequacy or inferiority. Erikson (1950) states that if a child "despairs of his tools and skills or of his status among his tool partners, her may be discouraged from identification with them", which may pull him back and result in isolation. In summary, if a child feels inadequate and incompetent in what he does, he will start to pull back and considers himself "doomed to mediocrity or inadequacy" (Erikson, 1950).

In the research, it is suggested that there are treatment related cognitive changes that children experience both throughout treatment and long term. Cognitive changes have become some of the most common and challenging problems associated with the

CNS-directed treatment for certain forms of cancer (Moore et al., 2013). This can lead to increasing gaps in their skills and knowledge compared to that of their classmates. This gap can greatly impact their development of either industry or inferiority. Industry is developed when a child can be confident and feel accomplished for tasks they are completing, while inferiority can develop when a child feels they are unable to accomplish tasks or be successful. With the gap in knowledge and skill that may be present in these children who have undergone chemotherapy, there is a significantly higher chance of them developing a sense of inferiority rather than the preferred sense of industry. These children will notice they are unable to keep up and begin to doubt themselves and their ability to be successful, further isolating them from their classmates.

Research Question

Based on what was reviewed and learned form the literature review, this study will investigate the following questions:

1. How is "Chemo Brain" (CB) defined by the pediatric oncology nurses who assess it?
2. According to the pediatric oncology nurses, what is the best evaluation of the severity of CB?
3. How do pediatric oncology nurses describe their best practices to teach/support patients and their families experiencing CB?
4. In conclusion, what are the best educational practices to teach about CB for families under stress with a child with cancer?

Methods

This is a qualitative/descriptive pilot study. In descriptive studies, there is no manipulation of variables, and the focus is describing a phenomenon. The use of a descriptive study design in this case is beneficial because for this is a pilot study this researcher is soliciting personal experiences and knowledge. Pilot study results will enable the researcher to determine if the instrument is valid for the proposed research questions. This design can help to discover specific variables to manipulate and include in future experimental research.

Subjects

Overall, the subjects of this study will be pediatric oncology registered nurses (RNs) practicing in hospitals throughout the state. A majority of the subjects will be members of the Bay Area/Northern California chapter of the Association of Pediatric Hematology/Oncology Nurses (BAHPON) who attend the chapter educational event on February 5, 2015. In addition to these nurses, other pediatric oncology RNs will be recruited as subjects for the study through snowballing.

Sampling Procedure

Primarily, convenience sampling will be used. Convenience sampling is a non-probability sampling technique where the research subjects are selected because of their convenient accessibility and proximity to the researcher, such as access to members of the BAHPON. With convenience sampling, the subjects are not representative of the entire population. Snowball sampling will also be used to obtain subjects for the study. Snowballing is also a non-probability sampling technique and may also be known as chain referral sampling. Researchers use this technique when the subjects may be hard to locate. Potential subjects are found through referral from existing subjects. In the case of

this study, snowballing is used to reach out to other pediatric oncology RNs that may not be members of BAHPON or may have not been in attendance at the meeting. The reason for non-probability sampling for this study is that childhood cancer is very rare and very few nurses select to work in this discipline. See Appendix A for a copy of the consent letter.

Sample Size

For a small pilot study, the nursing research literature encourages approximately 13-50 subjects or elements for each variable identified. The goal sample size for this study is 30 pediatric oncology RNs because the identified variables include assessment of presence and severity, and best practices for education. Purposeful sampling techniques will continue until the desired number of 30 is achieved or the date of March 1, 2015 dictates the completion of data collection.

Instruments

Research will be gathered through a survey given to pediatric oncology nurses. This instrument begins by inquiring demographic information about the subjects. It then asks both open-ended questions that explore RN's perceptions and practices related to CB and closed ended questions using a Likert scale. See Appendix B for a copy of the instrument.

Reliability

For this pilot study, the researcher is concentrating on the development of a valid instrument. When replicated, reliability will be tested using the techniques of Chronbach's Alpha.

Validity

Two advanced practice RNs in pediatric oncology will provide instrument construct and content validity. Construct validity is the extent to which inferences can be made from the operationalizations in the study to the theoretical constructs on which the operationalizations were based. Content validity refers to whether or not the items on the instrument truly test what the study is looking at, and that the instrument is representative of the research questions.

Step-by-Step Procedures

1. Receive IRB approval from the Dominican University of California Institutional Review Board.
2. Contact the president of BAPHON and request for permission to attend the February 5, 2015 meeting to give a short presentation of the study aims, methods, and time frame.
3. If allowed, attend BAPOHN meeting and hand out copies of instrument.
4. Request contact information of BAPOHN members for sending out another round of surveys to increase the amount of responses returned to primary investigator.
5. Contact and send out copies of the instrument to pediatric oncology nurses reached through snowballing.
6. Continue to send out copies of the instrument to members of the BAPOHN and other pediatric oncology nurses.
7. End collection of data on March 1, 2015.
8. Review all collected data.
9. Analyze the collected data.
10. Look for common themes in the open-ended responses.

11. Discuss the significance of the results.

Statistical Analysis

Pending

Results

Pending

Discussion

Pending

References

Evens, K., & Eschiti, V. (2009). Cognitive Effects of Cancer Treatment: "Chemo Brain" Explained. *Clinical Journal of Oncology Nursing, 13*(6), 661-666.

Duffner, P. (2009). Risk factors for cognitive decline in children treated for brain tumors. *European Journal of Paediatric Neurology, 14*, 106-115.

Moore, I., Hockenberry, M., & Krull, K. (2013). Cancer-Related Cognitive Changes in Children, Adolescents and Adult Survivors of Childhood Cancers. *Seminars in Oncology Nursing, 29*(4), 248-259.

Mulhern, R., & Palmer, S. (2003). Neurocognitive late effects in pediatric cancer. *Current Problems in Cancer,* 177-197.

Raffa, R., Duong, P., Finney, J., Garber, A., Pham, L., Matthew, S., ... Weng, H. (2006). Is 'chemo-fog'/'chemo-brain' caused by cancer chemotherapy? *Journal of Clinical Pharmacy and Therapeutics, 31*, 129-138.

Raffa, R. (2009). Is a picture worth a thousand (forgotten) words?: Neuroimaging evidence for the cognitive deficits in 'chemo-fog'/'chemo-brain' *Journal of Clinical Pharmacy and Therapeutics, 35*.

Staat, K., & Segatore, M. (2005). The Phenomenon Of Chemo Brain. *Clinical Journal of Oncology Nursing, 9*(6), 713-721.

Ullrich, N., & Embry, L. (2012). Neurocognitive dysfunction in survivors of childhood brain tumors. *Seminars in Pediatric Neurology*.

Appendix A

To Whom It May Concern:

My name is Jennifer Tapping and I am a senior nursing student at Dominican University of California. I am currently working on my senior thesis research study.

I would like to invite you to participate in a research study that will be conducted between December 2014 and March 2015, among pediatric oncology nurses. The project is titled, *"Nurse's Perceptions of Best Practices to Educate and Support Pediatric Patients and Their Families Experiencing "Chemo Brain:" A Pilot Study"*

Background: With more advanced and more aggressive chemotherapy cancer treatment leading to higher survival rates, complications with quality of life are becoming more prominent, especially delayed cognitive processing, commonly known as "Chemo Brain" (CB). At diagnosis and throughout treatment, patients and families are routinely educated about the plan of care, but according to oncology nurses' reports, too often details regarding the possibility of cognitive declines or deficits are left out.

Cognitive changes are some of the most common as well as challenging complications associated with central nervous system (CNS) directed treatment, such as intrathecal chemotherapy, for acute lymphoblastic leukemia (ALL) and brain tumors. The estimated incidence of patients who experience deficits in cognitive processing related to their CNS directed treatment is approximately 20% to 40% for children with ALL and 40% to 100% for children with brain tumors (Moore et al., 2013).

Purpose: The purpose of this study is three fold: 1) to define and discuss the etiology of CB, 2) to discuss the best assessment and evaluation of severity of CB, and 3) to explore pediatric oncology nurses' reports of best practice implications for teaching and supporting pediatric patients and their families experiencing CB.

Procedures: Data will be collected through a two-page survey instrument created by the researcher that has construct and content validity provided by two advanced practice registered nurses in pediatric oncology.

Risks: This research study has no potential risks.

Benefits: By participating in this research, further exploration and understanding of the best education and support practices related to CB in pediatric patients and their families may be reached. This may benefit the future practical implications related to CB.

Costs: There are no costs involved in this research study other than the time given completing the instrument.

Payments: There will be no payments for participation in this study.

Questions: If there are any questions about this study, the primary investigator, Jennifer Tapping, may be contacted by email at jennifer.tapping@students.dominican.edu. In addition, if there are concerns or any distress occurs as a result of this study, the research advisor, Dr. Luanne Linnard-Palmer, who is a practicing pediatric oncology nurse, may be contacted at (415)-257-1364

Consent: By completing the following instrument, **consent is implied**.

Thank you!

Appendix B

Nurse's Perceptions of Best Practices to Educate and Support Pediatric Patients and Their Families Experiencing "Chemo Brain:" A Pilot Study

Date:_____

Gender (circle one): Male Female Age:_____

Ethnicity:_____

Education Level:_____

Years in Nursing:_____

Years in Pediatric Hematology/Oncology_____

Have you seen children with the neurological/central nervous system (CNS) toxicity signs of "Chemo Brain" (CB)? (Circle one)

Yes No

How do you define CB?_____

_____

_____

How often do you see CB? (Circle one)

Never Almost Never Sometimes Almost Always Always

What primary symptom of CB have you seen?_____

_____

How often do you include the possibility of CB in your treatment consent procedures? (Circle one)

Never Almost Never Sometimes Almost Always Always

How do you describe/define CB to your patients and families?_____

_____

_____

_____

When does this discussion take place?_____

_____

How does your facility asses the presence of CB in your patients?_____

_____

_____

How does your facility assess the severity of CB in your patients?_____

_____

_____

In your opinion, what are the best educational practices to teach families under stress about CB?_____

_____

_____

Is there anything else about CB you would like to share?_____

_____

_____

_____

Thank you for your time!